## *REMARKS*

Applicant thanks Examiner Bunner for the discussion by telephone on October 28, 2003 on presentation of additional evidence to support the elected claims. Pursuant to these instructions, Applicant presents the additional evidence by way of a preliminary manuscript prepared by the inventor. Applicant also submits concurrently herewith a Declaration of Dr. Matthew During pursuant to 37 C.F.R. §1.132.

Claims 1-44, 47-69, and 77-109 are currently pending in this application. Claims 4, 13-21, 33-35, 47-53, 55-58, 62-67, 69 and 77-85 have been withdrawn in response to a restriction requirement. Claims 9-12, 26, 29-32, 41-46, 59-61, 70-76, 91-94, 98-101, and 105-108 have been canceled. In the Office Action dated May 5, 2003, the Examiner withdrew claims 1-3, 5-12, 22-32, 36-44, 54, 59-61, 68, and 86-108 and rejected claim 109.

Applicant respectfully request that the claims withdrawn by the Examiner in the Office Action dated May 5, 2003 be reinstated in light of the amendments made in this response. Claims 1, 6, 22, 24, 25, 27, 36, 38, 54, 68, 86, 95, and 102 have been amended so that the amended independent claims and corresponding dependent claims recite "administering a vaccine comprising a therapeutically effective amount of an antigen" as originally presented. Support for the amendments and new claim language can be found throughout the specification, and the claims as originally filed. No new matter has been added. Applicant reserves the right to file a divisional application for the non-elected claims or to reinstate certain claims upon the allowance of one or more generic claims.

Amendment of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to more particularly point out and distinctly claim the invention to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Applicants respectfully traverse the Examiner's rejections and request reconsideration of the application in view of the amendments made above and the remarks that follow.

***Election/Restriction***

In the Office Action of May 5, 2003, the Examiner asserts that Applicant's response filed February 11, 2003 was not responsive because the amended claims were directed to an invention that was patentably distinct from the invention that was already examined. The Office Action further states that:

> Group I was drawn to 'a method of treatment, improvement, or modification of a neurological disorder or protein comprising administering an *amino acid vaccine* comprising a therapeutically effective amount of antigen. . .'

In response, independent claims 1, 22, 36, 54, 86, 95, and 102 (and dependent claims thereof) have been amended to recite the language of the claims as originally presented and are directed to "*administering a vaccine* comprising a therapeutically effective amount of an antigen" as requested by the Examiner.

Furthermore, Applicant submits concurrently herewith a Declaration of Dr. Matthew During pursuant to 37 C.F.R. §1.132 and a manuscript entitled "Vaccination Against Distinct Domains of the NMDA Receptor Leads to a Preconditioned Phenotype Associated with Resistance to Seizures and Neuroprotection" to overcome the concerns expressed in the Office Action. This Declaration establishes that Applicant's claimed invention is directed to a method for modifying the function of a target receptor associated with a neurological disorder in a subject by administering a *vaccine* comprising a therapeutically effective amount of a peptide *antigen* in the circulatory system of the subject, wherein the *antigen elicits the production of antibodies* that, upon compromise of the blood-brain barrier, will pass into the central nervous system of the subject and bind to a target receptor located on a neuronal cell in the central nervous system of the subject and associated with a neurological disorder, and modify the function of the target receptor.

The Declaration provides evidence to support the concept that peptide antigens can elicit the production of antibodies, that these antibodies are present in the circulatory system, and that these antibodies are able to cross the blood-brain barrier and modify the function of the target

receptor as taught by the Applicant's specification. This modification of the target receptor can result in neuroprotection, improvement in cognitive function as well as neuroendocrine disorders that involve the same target receptor.

Based on these claim amendments and the Declaration, the Examiner is respectfully requested to reinstate the withdrawn claims.

***Rejection of Claim 109 under 35 USC § 112, First paragraph***

Claim 109 has been rejected under § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, the Office Action states that:

> "(i) ... no guidance or working examples in the specification to indicate that if administered, the NMDA *antigen* vaccine produces anti-NMDA antibodies and that the antibodies bind to a target receptor on a neuronal cell to directly modify the receptor or indirectly modify the function of a process involving the receptor *in vivo.*"

In light of the Declaration of Dr. Matthew During and the additional evidence provided in the manuscript entitled "Protein Vaccination Leading to a Preconditioned Phenotype Associated with resistance to Seizures and Neuroprotection," Applicant believes that claim 109 is fully enabled as discussed above. The results described in the manuscript clearly demonstrate that the teachings provided by the Applicant's specification are sufficient guidance for one skilled in the art to obtain similar results with the use of only routine experimentation. Routine experiments, described in the manuscript, were used to show that protein vaccination with peptide antigens of an N-methyl-D-aspartate (NMDA) receptor leads to neuroprotection and to resistance against seizures. Hence, the Applicant believes that the teachings of the specification are sufficient to allow one skilled in the art to practice the Applicants invention without undue experimentation.

The Office Action also asserts that:

> (ii)... Undue experimentation would be required of the skilled artisan to determine which specific neuronal cells express the appropriate target receptor and are also associated with a neurological disorder. Different types of neuronal cells express different populations of receptors and one skilled in the art cannot assume *that all neuronal cells in the central nervous system will express the target receptor recited in the claims*. (Emphasis added).

Applicant respectfully disagrees. Claim 109 is limited to those antibodies that "bind to a target receptor located on a neuronal cell in the central nervous system of the subject and associated with a [neurological] disorder." The claim does *not* cover any or all neuronal cells. On the contrary, the claim is only directed to neuronal cells that have the desired target receptor and that are associated with a neurological disorder, a neuroendocrine disorder, or cognition.

Furthermore, claim 109 does not require that all neuronal cells express the target receptor. Rather, the claim is drawn to a subset of neuronal cells that express the specific target receptor. It is only on these neuronal cells in which the receptor activity will be modified upon binding of the antibody. For example, not all neuronal cells will express the NMDA receptor, however a subset of neuronal cells do express the NMDA receptor, and it is on these cells that the NMDA receptor is modified by the binding of the NMDA antibody. Thus, any neurological, cognitive, or endocrine disorder that is associated with the NMDA receptor, can be effected by modifying the function of the NMDA receptor.

This same concept holds true for other receptors that are expressed on neuronal cells. For example, the Glutamate receptor (GluR) can be modified by antibodies that bind to the GluR receptor. This modification of the GluR receptor will in only occur in neuronal cells that express the GluR receptor, but not in other neuronal cells. Accordingly, Applicant respectfully requests that the Examiner withdraw this rejection.

With regard to the concern about the variety of target receptors associated with neurological disorders. The Office Action states that:

> (iii) Although one skilled in the art may be familiar with large numbers of receptors associated with neurological disease, undue experimentation would be required ....

Applicant respectfully disagrees. However, in order to expedite prosecution of the application, claims 6, 24, 25, and 38, have been amended to recite "a vaccine comprising an antigen derived from a neuroreceptor" and claim 68 has been amended to recite "the target receptor is a neuroreceptor." Claim 26 has been canceled. The claims therefore no longer recite a variety of target receptors, but simply a neuroreceptor, i.e., a receptor present on a neuronal cell. Accordingly, the Examiner is respectfully requested to withdraw the rejection.

## CONCLUSION

In summary, the above-identified patent application has been amended and reconsideration is respectfully requested for all the reasons set forth above. The Examiner is urged to telephone the undersigned Attorney for Applicant in the event that such communication is deemed to expedite prosecution of this matter.

Respectfully submitted,

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